UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/615,615	07/08/2003	Clemens Hendricus, M. Kocken	2183-6041US	8276

24247 7590 06/11/2010

TRASKBRITT, P.C.
P.O. BOX 2550
SALT LAKE CTY, UT 84110

EXAMINER	
HIBBERT, CATHERINE S	

ART UNIT	PAPER NUMBER
1636	

NOTIFICATION DATE	DELIVERY MODE
06/11/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTOMail@traskbritt.com

Office Action Summary	Application No.	Applicant(s)	
	10/615,615	KOCKEN ET AL.	
	Examiner	Art Unit	
	CATHERINE HIBBERT	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,8-10,27-30 and 46-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 8-10, 27-30, and 46-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 March 2010 has been entered.

Applicant's Amendments to the Claims, filed 22 March 2010, have been received and entered. Claims 2, 4-7, 11-26 and 31-45 are cancelled. Claims 1, 3, 8-10, 27-30, and 46-49 are pending and under consideration in this action.

Response to Amendment/Arguments

Any objections/rejections not repeated in this action are withdrawn herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 8-10, 46, 48, 49 STAND rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record and presented herein. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection of cancelled claims 2 and 4 is moot.

Applicants claim a method for producing mRNA encoding a *Plasmodium falciparum* apical membrane antigen-1 (AMA-1) ectodomain or a fragment thereof in a yeast cell, said method comprising: providing said yeast cell with a nucleic acid encoding the ectodomain or the fragment thereof, wherein the ectodomain *comprises* amino acid sequences 25-545 of SEQ ID NO:7, and wherein the fragment thereof *comprises* an amino acid sequence from among 25-442, 97-442, and 97-545 of SEQ ID NO: 7, and wherein the nucleic acid encoding the ectodomain or the fragment thereof has been modified to utilize the yeast cell's codon usage, and wherein mAB 4G2 exhibits specificity for the ectodomain or the fragment thereof; expressing the nucleic acid in the yeast cell, thus making the mRNA encoding the ectodomain or the fragment thereof, and wherein the nucleic acid encoding the fragment encodes a peptide consisting of an amino acid sequence selected from the group of amino acid sequences consisting of amino acids 25-442, 97-442, and 97-545 of SEQ ID NO: 7. Thus, the claims read on a method that employs a broad genus of sequences.

The written description requirement for a genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicants were in possession of the

claimed invention. In the instant case, the specification does not sufficiently describe a representative number of functional nucleic acids by actual reduction to practice or by disclosure of relevant identifying characteristics.

Thus, the nucleic acid biomolecules encoding the ectodomains and ectodomain fragments are a critical element to Applicants invention, as claimed, as directed to methods for producing mRNAs and ectodomains and ectodomain fragments. While Applicants show written description for nucleic acids encoding the amino acid sequence of SEQ ID NO: 7 and the explicitly designated fragments thereof that produce the amino acid sequences consisting of amino acids 25-442, 97-442, and 97-545 of SEQ ID NO: 7, Applicant does not show possession of the claimed method of producing functional mRNAs that produce properly folded proteins that would be specifically recognized by the mAB 4G2 that encompass the myriad of broad species of nucleic acids encompassed by the claims. The claims, as written, are drawn to a nucleic acid encoding specific ectodomains but do not actually limit the expression products to these designated peptides. The determination of which potential nucleic acids would be functional and correlate to the production of properly folded proteins that would be specifically recognized by the mAB 4G2 would not be predictable and would have to be determined empirically by experimentation involving live yeast cells.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals

appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the *entire scope* of the claimed invention.

Applicants response is to traverse the rejection. Applicants' have amended claims 1, 27, and 46-48. Applicants argue:

> Applicants respectfully note that a sequence can meet the written description requirement under *Enzo Biochem, Inc. v. Gen-Probe Inc.* through the showing "relevant identifying characteristics i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. 296 F.3d 1316, 1324 (Fed. Cir. 2002) (emphasis added). Applicants respectfully note that added emphasis on "or" which applicants submit clearly indicates that one does not have to meet each and every one of the test outlined by the *Enzo* court, but that any one of them can be met to satisfy the written description requirement.

Applicants further note that:

> the genus of "variants" can also be provided with adequate written description "through sufficient description of a representative number of species by actual reduction to practice." M.P.E.P. § 2163(II)(A)(3)(a)(ii) Further "what constitutes a 'representative number' is an inverse function of the skill and knowledge in the art." Id. Applicants respectfully submit that the skill and knowledge concerning nucleotides sequences in the biotechnological arts is very high.

Applicants further submit that "one of ordinary skill in the arts would readily conclude that the applicants were in possession of a common attribute possessed by members of the genus;... See, e.g., M.P.E.P. § 2163(II)(A)(3)(a)(ii)". In addition, Applicants argue:

> Although applicants do not agree that any of the claims lack written description, to expedite prosecution, the claims have been amended herein. Specifically, the

claims have been amended to recite that the at least one glycosylation site that has been removed is an N- glycosylation site.

The Office states, on page 7 of the Final Office Action of November 25, 2009, that while the applicants are in possession of SEQ ID NO:7 and the designated fragments thereof, the applicants do not show possession of species which require "unknown modifications" to the amino acid SEQ ID NO:7. Specifically the Office asserts that the determination of which potential amino acid sequence modification that would be encompassed by the claims requiring removal of glycosylation sites and correlate to the production of properly folded proteins would not be predictably. Applicants respectfully disagree.

Applicants further argue:

The presently claimed methods provide AMA-1 ectodomains or designated fragments thereof that have been modified to remove at least one N-glycosylation site. Furthermore, mAb 4G2 exhibits specificity for said ectodomains or fragments. As described at ¶ 100151 of the Specification, AMA-1 contains six N-glycosylation sites that are potentially recognized by eukaryotic systems. A person of ordinary skill in the art at the time of the invention would have been aware of the N-glycosylation consensus sequence. The application further describes in the same paragraph how at least one of the six sites may be removed. The claims therefore define sequences that can be predictably modified at six sites to remove at least one N-glycosylation site.
As noted by the Office, a genus can be adequately described if the disclosure presents a sufficient number of representative species. Description of a representative number of species does not require that the description to be of such specificity that it would provide individual support for each species that the genus embraces, and what constitutes a "representative number" is an inverse function of the skill and knowledge in the art. M.P.E.P. § 2163 (II)(A)(3)(a); In re Bell, 991 F.2d 781,785 (Fed. Cir. 1993); In re Baird, 16 F.3d 380, 382 (Fed. Cir. 1994).

Further, Applicants submit:

Applicants have provided working examples for the removal of all six potential glycosylation sites (see, e.g., ¶ 100471). Applicants have further shown that modification of these six sites results in an AMA-1 ectodomain that is properly folded and can react with mAb 4G2 (see, e.g., ¶ 10051]). A person of ordinary skill in the art, at the time of the invention, would thus have concluded that none of the potential N-glycosylation sites is required for proper folding and that these sites can be modified without affecting the conformation or the ability to react with mAb 4G2.

Satisfactory disclosure of a "representative number" depends on whether one of ordinary skill in the art at the time of the invention would have recognized that the applicants were in possession of the necessary common attributes or features of the element possessed by the members of the genus in view of the species disclosed. See, e.g, Eli Lilly. As applicants have successfully modified all six potential N-glycosylation sites, a person of ordinary skill in the art at the time of the invention would have necessarily recognized that the applicants were in possession of a representative number of species.

In addition, Applicants argue:

In the previous response of the applicants, several arguments were made regarding the Fandeur reference cited by the Office in the Office Action of April 1, 2009, namely that Fandeur provides no suggestion of unpredictability in AMA-1 variants or in producing properly folding protein and that Fandeur suggests that while there may be some different effects by the strains, there is predictability that transcends strain diversity. The Office has stated in the present Final Office Action that applicants arguments are not found persuasive, however the Office has failed to state the reasons for this decision (see 37 C.F.R. § 1.113). Fandeur describes Plasmodium variants that differ from each other in a number of characteristics (see bridging paragraph 225- 226). Fandeur however, is silent regarding AMA-1 and fails to suggest unpredictably of the claimed subject matter.

The Office states that the claims require experimentation to determine which modified nucleic acids would encode polypeptides that would be folded correctly. Applicants fail to understand the relevance of this statement in the determination of compliance with the written description requirement. Nevertheless, any experimentation required by a skilled person to practice the claimed invention is merely routing, is guided by the specification, and is not an undue burden.

The Office further asserts that the claims use the open language "comprising" and as such do not expressly limit the ectodomain. The disclosure teaches one of skill in the art that the AMA-1 ectodomains that are necessary for reactivity with mAb 4G2, namely domain I or domains I + II. This domain(s) is required for reactivity, however, and nothing in the disclosure or the art suggest that additional sequences would interfere with proper folding of the protein. As one example, Table 2 demonstrates that antigen Pf 11-0 having AMA-1 residues 25-545 is properly folded. Therefore, ectodomain fragments such as 97-442, can clearly encompass additional amino acids and still fold properly. However, in an effort to expedite prosecution, the claims have been amended to recite fragments consisting of the particular amino acid sequences.
Furthermore, the Office states that claim 49 does not refer to any specific amino

> acid fragment. Claim 49 is amended herein to refer to amino acids 97-442 of SEQ ID NO:7. The Office also states that the claims are directed to nucleic acids and not to polypeptide fragments.

Applicants further state that the "claims are amended herein to refer to the amino acid sequence of the ectodomain and the fragments" and submit:

> An objective standard for determining compliance with the written description requirement is: "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." In re Gosteli, 872 F.2d 1008, 1012 (Fed. Cir.1989). The disclosure provides working examples of AMA-1 ectodomain and fragments that have been modified 1) to remove all six potential N-glycosylation sites and 2) to utilize the yeast cell's codon usage. The working examples demonstrate good protein expression, proper folding, and are reactive to mAb 4G2.

Thus, Applicants submit that "one of ordinary skill in the art at the time of the invention would have reasonably concluded that applicants possessed the claimed subject matter". Applicants further submit that "this conclusion is buttressed by the level of skill and knowledge of art at the time of the invention and the representative number of species disclosed in supporting the scope of the claims".

Applicants' arguments have been fully considered but are respectfully not found persuasive for reasons of record and presented herein. Examiner acknowledges the Applicants' amendment to the base claims 1, 27, 46, 47, 48 and 49 which removes the claim language pertaining to "wherein at least one glycosylation site has been removed" and that these amendments render the arguments pertaining to this limitation moot. In addition, Examiner acknowledges the Applicants' amendment to the base claims 1, 27, 46, 47, 48 and 49 that adds the claim language "wherein the nucleic acid encoding the fragment encodes a peptide consisting of an amino acid sequence selected from the group of amino acid sequences consisting of amino acids 25-442, 97-

442, and 97-545 of SEQ ID NO: 7". However, it is noted that the addition of the "consisting" closed language does not actually further limit the claimed nucleic acids because the nucleic acids are only required to "encode" the various amino acid fragments but not to produce the various amino acid fragments. For example, a full-length nucleic acid would be considered to encode all the variations or fragments encompassed by the encoding sequence and therefore a description of what fragments a nucleic acid could encode would not be the same as a description of what mRNAs would be produced by the nucleic acid. Therefore, the claims require experimentation to determine which nucleic acids would produce the required mRNAs that would express the required ectodomains and fragments that would be folded correctly for specific recognition by the mAb 4G2. Therefore, applicants' arguments are not commensurate with the scope of the claims, as written, as the arguments are directed at nucleic acids that produce specific mRNAs rather than nucleic acids that encode specific mRNAs. Examiner notes that currently amended claim 47, for example, is remedial with respect to providing appropriate written description for the scope of the claims but is rejected under a different grounds for new matter, see just below.

New grounds of rejection necessitated by amendment

Claim 47 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **NEW MATTER** rejection.

Currently amended claim 47 recites wherein the fragment peptide consists of an amino acid sequence consisting of amino acids "96-545" of SEQ ID NO:7 in lines 12-13. The instant specification does not refer to a peptide fragment species that consists of an amino acid sequence consisting of amino acids "96-545" of SEQ ID NO:7.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 8-10, 27-30, 46 and 48-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 27 recites the limitation "the mRNA" in line 11. There is insufficient antecedent basis for this limitation in the claim because there is no reference to an mRNA previously in the claim.

Claims 28-30 and 48 are indefinite insofar as they depend from Claim 27.

In addition, currently amended claims 1, 46, 48 and 49 are indefinite because the claims appear to list the two active method steps of "providing" and "expressing" but have deleted out the conjunctive term "and" between the steps and have added a new conjunctive term "and" following the second active method step but without adding a third active method step, and therefore it is unclear whether the sentence is a grammatically complete sentence.

Claims 3, 8, 9, 10 are indefinite insofar as they depend from claim 1.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHERINE HIBBERT whose telephone number is (571)270-3053. The examiner can normally be reached on M-F 8AM-5PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Catherine Hibbert
Examiner AU1636

/NANCY VOGEL/
Primary Examiner, Art Unit 1636